Potential bioterrorism agent: Category A

TULAREMIA

DISEASE REPORTING

In Washington

DOH receives 2 to 8 reports of tularemia infections per year.

Exposures identified in Washington cases include farming and rabbit skinning.

Purpose of reporting and surveillance

- To assist in diagnosis.
- When the source is a risk for only to a few individuals (e.g., animal exposure), to inform those individuals how they can reduce their risk of exposure.
- To educate potentially exposed persons about signs and symptoms of disease, thereby facilitating early diagnosis.
- To identify potentially exposed laboratory personnel and to provide counseling.
- To raise the index of suspicion of a possible a bioterrorism event if no natural exposure source is identified.

Reporting requirements

- Health care providers: notifiable to Local Health Jurisdiction within 3 work days
- Hospitals: notifiable to Local Health Jurisdiction within 3 work days
- Laboratories: specimen submission required
- Local health jurisdictions: notifiable to DOH Communicable Disease Epidemiology within 7 days of case investigation completion or summary information required within 21 days. ***If bioterrorism is suspected, case must be immediately reported to DOH: 1-877-539-4344***

CASE DEFINITION FOR SURVEILLANCE

Clinical criteria for diagnosis

An illness characterized by several distinct forms, including the following:

- Ulceroglandular (cutaneous ulcer with regional lymphadenopathy)
- Glandular (regional lymphadenopathy with no ulcer)
- Oculoglandular (conjunctivitis with preauricular lymphadenopathy)
- Oropharyngeal (stomatitis or pharyngitis or tonsillitis and cervical lymphadenopathy)
- Intestinal (intestinal pain, vomiting, and diarrhea)
- Pneumonic (primary pleuropulmonary disease)

- Typhoidal (febrile illness without early localizing signs and symptoms).

Clinical diagnosis is supported by evidence or history of a tick or deerfly bite, exposure to tissues of a mammalian host of *Francisella tularensis*, or exposure to potentially contaminated water.

Laboratory criteria for diagnosis

Presumptive

- Elevated serum antibody titer(s) to *F. tularensis* antigen (without documented fourfold or greater change) in a patient with no history of tularemia vaccination, or
- Detection of *F. tularensis* in a clinical specimen by fluorescent assay.

Confirmatory

- Isolation of *F. tularensis* in a clinical specimen, or
- Fourfold or greater change in serum antibody titer to *F. tularensis* antigen.

Case definition

- Probable: a clinically compatible case with laboratory results indicative of presumptive infection.
- Confirmed: a clinically compatible case with confirmatory laboratory results.

A. DESCRIPTION

1. Identification

A zoonotic bacterial disease with a variety of clinical manifestations related to the route of introduction and the virulence of the disease agent. Most often it presents as an indolent ulcer at the site of introduction of the organism, together with swelling of the regional lymph nodes (ulceroglandular type). There may be no apparent primary ulcer, but only one or more enlarged and painful lymph nodes that may suppurate (glandular type). Ingestion of organisms in contaminated food or water may produce a painful pharyngitis (with or without ulceration), abdominal pain, diarrhea and vomiting (oropharyngeal type). Inhalation of infectious material may be followed by pneumonic involvement or a primary septicemic syndrome with a 30%-60% case-fatality rate if untreated (typhoidal type); bloodborne organisms may localize in the lung and pleural spaces (pleuropulmonary type). The conjunctival sac is a rare route of introduction that results in a clinical disease of painful purulent conjunctivitis with regional lymphadenitis (oculoglandular type). Pneumonia may complicate all clinical types and requires prompt identification and specific treatment to prevent a fatal outcome.

Two biovars with differing pathogenicity cause human disease. Jellison type A organisms are more virulent, with an untreated case-fatality rate of 5%-15% primarily due to typhoidal or pulmonary disease. With appropriate antibiotic treatment, the case-fatality

rate is negligible. Jellison type B organisms are less virulent and, even without treatment, produce few fatalities. Clinically, because of buboes and/or severe pneumonia, tularemia may be confused with plague, as well as many other infectious diseases, including staphylococcal and streptococcal infections, cat-scratch fever and sporotrichosis.

Diagnosis is most commonly made clinically and confirmed by a rise in specific serum antibodies that usually appear in the second week of the disease. Cross-reactions occur with *Brucella* species. Examination of ulcer exudate, lymph node aspirates and other clinical specimens by FA test may provide rapid diagnosis. Diagnostic biopsy of acutely infected lymph nodes should be done only under the cover of specific antibiotic treatment since it will often induce bacteremia. The causative bacteria can be cultured on special media such as cysteine-glucose blood agar or by inoculation of laboratory animals with material from lesions, blood or sputum. The biovars are differentiated by their chemical reactions; type A organisms ferment glycerol and convert citrulline to ornithine. Extreme care must be exercised to avoid laboratory transmission of highly infectious aerosolized organisms; hence, culture identification is performed only in reference laboratories and most cases are diagnosed serologically.

2. Infectious Agent

Francisella tularensis (formerly *Pasteurella tularensis*), a small, gram-negative nonmotile coccobacillus. All isolates are serologically homogeneous but are differentiated epidemiologically and biochemically into Jellison type A (*F. tularensis* biovar *tularensis*), which has an LD50 in rabbits of fewer than 10 bacteria, or type B strains (*F. tularensis* biovar *palaearctica*), which have an LD50 of greater than 107 in rabbits.

3. Worldwide Occurrence

Tularemia occurs throughout North America and in many parts of continental Europe, the former Soviet Union, China and Japan. In the US, it occurs in all months of the year; incidence may be higher in adults in early winter during rabbit hunting season and in children during the summer when ticks and deer flies are abundant. *F. tularensis* biovar tularensis organisms, restricted to North America, are common in rabbits (cottontail, jack and snowshoe), and are frequently transmitted by tick bite. *F. tularensis* biovar palaearctica strains are commonly found in mammals other than rabbits in North America; strains in Eurasia are found in voles, muskrats and water rats; and in rabbits in Japan.

4. Reservoir

Numerous wild animals, especially rabbits, hares, voles, muskrats, beavers and some domestic animals; also various hard ticks. In addition, a rodent-mosquito cycle has been described for *F. tularensis* biovar palaearctica in Scandinavia, the Baltic states and Russia.

5. Mode of Transmission

Through the bite of arthropods, including the wood tick *Dermacentor andersoni*, the dog tick *D. variabilis*, the lone star tick *Amblyomma americanum*, less commonly the deer fly *Chrysops discalis* and, in Sweden, the mosquito *Aedes cinereus*; by inoculation of skin, conjunctival sac or oropharyngeal mucosa with contaminated water, blood or tissue while handling carcasses of infected animals (e.g., skinning, dressing or performing necropsies); by handling or ingesting insufficiently cooked meat of infected animal hosts; by drinking contaminated water; by inhalation of dust from contaminated soil, grain or hay; rarely, from bites of coyote, squirrel, skunk, hog, cat and dog whose mouth presumably was contaminated from eating an infected animal; and from contaminated pelts and paws of animals. Laboratory infections occur and frequently present as a primary pneumonia or typhoidal tularemia.

6. Incubation period

Related to virulence of infecting strain and to size of inoculum; the range is 1-14 days, usually 3-5 days.

7. Period of communicability

Not directly transmitted from person to person. Unless treated, the infectious agent may be found in the blood during the first 2 weeks of disease and in lesions for a month, sometimes longer. Flies can be infective for 14 days and ticks throughout their lifetime (about 2 years). Rabbit meat frozen at -15°C (5°F) has remained infective longer than 3 years.

8. Susceptibility and resistance

All ages are susceptible, and long-term immunity follows recovery; however, reinfection has been reported in laboratorians.

B. METHODS OF CONTROL

1. Preventive measures:

a. Educate the public to avoid bites of ticks, flies and mosquitoes and to avoid drinking, bathing, swimming or working in untreated water where infection prevails among wild animals.
b. Use impervious gloves when skinning or handling animals, especially rabbits. Cook the meat of wild rabbits and rodents thoroughly.
c. Prohibit interstate or interarea shipment of infected animals or their carcasses.
d. Live attenuated vaccines applied intradermally by scarification are used extensively in the former Soviet Union, and to a limited extent for occupational risk groups in the

US. Such an investigational live attenuated vaccine for laboratory personnel working with the organism is no longer available in the US.

e. Wear face masks, gowns and impervious gloves and negative pressure microbiological cabinets when working with cultures of *F. tularensis*.

2. Control of patient, contacts and the immediate environment:

a. Report to local health authority.
b. Isolation: Drainage and secretion precautions for open lesions.
c. Concurrent disinfection: Of discharges from ulcers, lymph nodes or conjunctival sacs.
d. Quarantine: None.
e. Immunization of contacts: Not indicated.
f. Investigation of contacts and source of infection: Important in each case, with search for the origin of infection.
g. Specific treatment: Streptomycin or gentamicin given for 7-14 days is the drug of choice; the tetracyclines and chloramphenicol are bacteriostatic and effective when continued for no less than 14 days; relapses are reported to occur more often than with streptomycin. Moreover, fully virulent streptomycin-resistant organisms have been described. Aspiration, incision and drainage, or biopsy of an inflamed lymph node can spread the infection and must be covered with prompt and specific antibiotics. See also: Dennis DT, Inglesby TV, Henderson DA, et al. Tularemia as a biological weapon: medical and public health management. JAMA 2001; 285:2763-73 (in *Additional Resources*).

3. Epidemic measures

Search for sources of infection related to arthropods, animal hosts, water, soil and crops. Control measures as indicated in B1, above.

4. International measures

None.

6. Bioterrorism measures

Tularemia is considered to be a potential biowarfare/bioterrorist agent, particularly if used as an aerosol threat. As is true of plague, cases acquired by inhalation would present as primary pneumonia. Such cases require prompt identification and specific treatment to prevent a fatal outcome. All diagnosed cases of pneumonia due to *F. tularensis*, especially any cluster of cases should be reported immediately to the local health department for appropriate investigations.